

## WHAT IS CLAIMED IS:

1. A method for aiding in the diagnosis or monitoring of Alzheimer's disease in a patient, said method comprising:
  - measuring the amount of one or more soluble  $A\beta(x \geq 41)$  in a patient sample;
  - comparing the measured amount with a predetermined amount of said one or more soluble  $A\beta(x \geq 41)$ ; and
  - assessing patient status based on a difference between the measured and predetermined amounts.
2. A method as in claim 1, wherein the predetermined amount of  $A\beta(x \geq 41)$  is an indicator value and wherein a measured amount above the indicator value provides a negative indication in the diagnosis of Alzheimer's disease and a measured amount at or below the indicator value provides a positive indication in the diagnosis of Alzheimer's disease.
3. A method as in claim 2, wherein the patient sample is CSF and the indicator value is between about 0.45 ng/ml and about 0.7 ng/ml.
4. A method as in claim 2, wherein the patient sample is CSF and the indicator value is about 0.5 ng/ml.
5. A method as in claim 4, wherein the  $A\beta(x \geq 41)$  measured contain at least  $A\beta$  amino acids 33-41.
6. A method as in claim 1, wherein the predetermined amount is a value measured from the same patient at an earlier time and the method provides for monitoring.
7. A method as in claim 1, wherein the amount of soluble  $A\beta(x \geq 41)$  is measured by exposing the patient sample to a first binding substance specific for a junction region on  $A\beta$  or  $A\beta$  fragment disposed between amino acid residues 13 to 26

and detecting binding between the first binding substance and  
5 the soluble  $A\beta(x \geq 41)$  by exposing the patient sample to a  
second binding substance specific for  $A\beta(x \geq 41)$ .

8. A method of claim 7 wherein the second binding substance is an antibody recognizing an epitope on  $A\beta$  having amino acid residues 33-42.

9. A method as in claim 8, wherein the first binding substance is an antibody recognizing an epitope on  $A\beta$  having amino acid residues 13-26.

10. A method as in claim 9, wherein binding of the first binding substance and the soluble  $A\beta(x \geq 41)$  is detected by separating bound complexes of the binding substance and  $A\beta$ s or  $A\beta$  fragments, exposing the separated bound complexes to a labeled second binding substance specific for  $A\beta(x \geq 41)$ , and  
5 detecting the presence of label on the bound complexes.

11. A method for detecting a soluble amyloid- $\beta$  peptide( $x \geq 41$ ) ( $A\beta(x \geq 41)$ ) in a fluid sample, said method comprising:

capturing soluble  $A\beta(x \geq 41)$  from the sample using a first binding substance specific for a junction region on  $A\beta$ ;  
5 and

detecting capture of soluble  $A\beta(x \geq 41)$  using a labeled second binding substance specific for  $A\beta(x \geq 41)$ .

12. A method as in claim 11, wherein the fluid sample is cerebrospinal fluid.

13. A method as in claim 11, wherein the soluble  $A\beta(x \geq 41)$  is captured on a solid phase, and the capture is detected by exposing the solid phase to the labeled second binding substance and thereafter detecting the presence of the label on the solid phase.

14. A system for detecting soluble amyloid- $\beta$  peptide( $x \geq 41$ ) ( $A\beta(x \geq 41)$ ) in a fluid sample, said system comprising:

a first binding substance specific for an epitope in a junction region of  $A\beta$  between amino acid residues 13-26; and a  
5 second binding substance specific for an epitope of  $A\beta(x \geq 41)$  but that does not cross react with an epitope of  $A\beta(\leq 40)$ ;

wherein one of the first and second binding substances is bound to a solid phase and the other is labeled.

15. A system as in claim 14, wherein the second binding substance is specific for an epitope having amino acids 33-42 of  $A\beta$ .

16. A system as in claim 14, wherein the first binding substance is bound to a solid phase and the second binding substance is labeled.

17. A system as in claim 14, wherein the first and second binding substances are antibodies.

18. A system as in claim 14, wherein the second binding substance is bound to an enzyme label.

19. A system as in claim 18, further comprising substrate for the enzyme.

20. A method for screening a compound to determine its ability to alter the amount of  $A\beta(x \geq 41)$  in the CSF comprising:

measuring a first amount of one or more soluble  $A\beta(x \geq 41)$  in the CSF of a non-human animal used as a model of  
5 Alzheimer's disease;

administering the compound to the non-human animal;  
measuring a second amount of said one or more soluble  $A\beta(x \geq 41)$  in the CSF of the non-human animal; and

10 comparing the first amount with the second amount,  
the difference indicating whether the compound  
increases, decreases, or leaves unchanged the amount of soluble  
 $A\beta(x \geq 41)$  in the CSF.

21. The method of claim 20 wherein the non-human  
animal is a rodent.

22. The method of claim 21 wherein the rodent is a  
mouse.

23. A method for aiding in the diagnosis or  
monitoring of Alzheimer's disease in a patient, said method  
comprising:

measuring the amount of one or more soluble  $A\beta(x \geq 41)$   
in a patient sample;

5 comparing the measured amount with a predetermined  
amount of said one or more soluble  $A\beta(x \geq 41)$ ;

measuring the amount of tau in a patient sample;

comparing the measured amount with a predetermined  
amount of said tau; and

10 assessing patient status based on a difference between  
the measured and predetermined amounts of  $A\beta(x \geq 41)$  and tau.

24. A method as in claim 23, wherein the  
predetermined amount of  $A\beta(x \geq 41)$  and tau are indicator values  
and wherein a measured amount at or below the  $A\beta(x \geq 41)$   
indicator value and at or above the tau indicator value  
provides a positive indication in the diagnosis of Alzheimer's  
5 disease, and wherein a measured amount above the of the  $A\beta(x \geq 41)$  indicator value and below the tau indicator value  
provides a negative indication in the diagnosis of Alzheimer's  
disease.

25. A method as in claim 24, wherein the patient  
sample is CSF, the indicator value for  $A\beta(x \geq 41)$  is between

about 0.45 ng/ml and about 0.7 ng/ml and the indicator value for tau is about 0.25 ng/ml and about 0.4 ng/ml.

26. A method as in claim 24, wherein the patient sample is CSF and the indicator value is about 0.5 ng/ml and the indicator value for tau is about 0.3 ng/ml.

27. A method as in claim 26, wherein the  $A\beta(x \geq 41)$  measured contain at least  $A\beta$  amino acids 33-41.

28. A method as in claim 23, wherein the predetermined amounts are values measured from the same patient at an earlier time and the method provides for monitoring.

29. A method as in claim 23, wherein the amount of soluble  $A\beta(x \geq 41)$  is measured by exposing the patient sample to a first binding substance specific for a junction region on  $A\beta$  or  $A\beta$  fragment disposed between amino acid residues 13 to 26 and detecting binding between the first binding substance and  
5 the soluble  $A\beta(x \geq 41)$  by exposing the patient sample to a second binding substance specific for  $A\beta(x \geq 41)$ .

30. A method of claim 29 wherein the second binding substance is an antibody recognizing an epitope on  $A\beta$  having amino acid residues 33-42.

31. A method as in claim 30, wherein the first binding substance is an antibody recognizing an epitope on  $A\beta$  having amino acid residues 13-26.

32. A method as in claim 31, wherein binding of the first binding substance and the soluble  $A\beta(x \geq 41)$  is detected by separating bound complexes of the binding substance and  $A\beta$ s or  $A\beta$  fragments, exposing the separated bound complexes to a labeled second binding substance specific for  $A\beta(x \geq 41)$ , and  
5 detecting the presence of label on the bound complexes.

33. A method for screening a compound to determine its ability to alter the amount of both  $A\beta(x \geq 41)$  and tau in the CSF comprising:

- measuring a first amount of one or more soluble  $A\beta(x \geq 41)$  in the CSF of a non-human animal used as a model of Alzheimer's disease;
- measuring a first amount of tau in the CSF of the non-human animal;
- administering the compound to the non-human animal;
- measuring a second amount of said one or more soluble  $A\beta(x \geq 41)$  in the CSF of the non-human animal;
- measuring a second amount of tau in the CSF of the non-human animal; and
- comparing the first amounts with the second amounts, the difference indicating whether the compound increases, decreases, or leaves unchanged the amount of soluble  $A\beta(x \geq 41)$  and increases, decreases, or leaves unchanged the amount of tau in the CSF.

34. The method of claim 33 wherein the non-human animal is a rodent.

35. The method of claim 34 wherein the rodent is a mouse.

36. A kit comprising a binding substance that binds  $A\beta(x \geq 41)$  but that does not bind to  $A\beta(\leq 40)$  and a binding substance that binds to tau.

37. The kit of claim 36 further comprising a binding substance that binds  $A\beta$  or a fragment of  $A\beta$  but that does not bind other fragments of APP.

38. The kit of claim 37 wherein the binding substance that binds  $A\beta(x \geq 41)$  but that does not bind to  $A\beta(\leq 40)$  binds to an epitope containing amino acids beyond number 40 in  $A\beta$  and

the binding substance that binds A $\beta$  or a fragment of A $\beta$  but  
that does not bind other fragments of APP binds to the junction  
5 region of A $\beta$ .

39. The kit of claim 38 comprising a) an un-labeled  
binding substance that binds to the junction region of A $\beta$ ; b)  
a detectably labelled binding substance that binds to an  
epitope containing amino acids beyond number 40 in A $\beta$ ; c) an  
un-labelled binding substance that binds to tau; and d) a  
5 detectably labelled binding substance that binds to tau.

40. The kit of claim 39 wherein the binding  
substances are antibodies.

41. The kit of claim 40 wherein the antibodies are  
monoclonal antibodies.

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